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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 04/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/754,732	HAAN ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 13-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 13-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/403,139.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8 January 2004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 13-19 are presented for examination.

The present application is acknowledged as a continuation of U.S. Application No. 10/303,494 filed November 25, 2002, now abandoned, which is a continuation of U.S. Application No. 10/117,899 filed April 6, 2002, now U.S. Patent No. 6,514,958, issued February 4, 2003, which is a continuation of U.S. Application No. 09/403,139 filed October 14, 1999, now U.S. Patent No. 6,399,594, issued June 4, 2002, which is a proper National Stage (371) entry of PCT Application No. PCT/EP98/02361, filed April 20, 1998, which claims foreign priority to European Patent 97201180.3 filed April 22, 1997.

Applicant's Preliminary Amendment filed January 8, 2004 has been received and entered into the application. Accordingly, claims 1-12 have been cancelled, claims 13-19 have been added and the specification at page 1, line 1 and page 13, line 21 has been amended. Applicant's amendment filed May 13, 2004 has also been received and entered into the application. Accordingly, the obvious error in the filing date of U.S. Application No. 10/117,899 in the specification at page 1, lines 3-4 has been amended.

Applicant's Information Disclosure Statement filed January 8, 2004 has been received and entered into the application. As reflected by the attached, completed copy of form PTO-1449 (1 page total), the Examiner has considered the cited references.

Specification

The Examiner has noted the incorporation by reference of European Patent 389035 at page 1, line 9 of the disclosure. The incorporation of essential material in the specification by

reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by a statement executed by the Applicant, or a practitioner representing the Applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. See 37 CFR 1.57(f).

The use of the trademark LIVIAL® has been noted in this application at page 1, line 10 of the disclosure. Each letter should be capitalized and be accompanied by the generic terminology wherever it appears. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks.

The disclosure is objected to because of the following minor informalities:

(i) the amount of tibolone recited at page 1, line 15 should read ---**2.5 mg**---; and

(ii) the phrase "...advantage being manifest particularly..." at page 2, line 28 should be changed to read "...advantage **is manifested** particularly..." for clarity.

Appropriate correction is required.

Claim Interpretation

The present claims comply fully with 35 U.S.C. § 112, first and second paragraph. The Examiner wishes to note, however, that while it appears that Applicant intends the amount of tibolone in present claim 13 to be based on the weight of the entire dosage unit (e.g., see the present specification at page 2, lines 16-19), one could construe the claimed amount to be based on the weight of the capsule itself, i.e., the gelatin material which encloses the active agent and

carrier materials, and, thus, interpret the amount of tibolone to be much less than intended by Applicant. In the rejections set forth below, the Examiner has interpreted the claimed amounts of tibolone to be based on the dosage form as a whole.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kelder et al. (U.S. Patent No. 4,701,450; 1987) in view of Deckers et al. (EP 0613687; 1994), Handbook of Pharmaceutical Excipients (1986, p.108-110, 259-260, 289-293), Loliger et al. (U.S. Patent No. 5,364,886; 1994) and Sas et al. (EP 0389035; 1990).

Kelder et al. teaches a pharmaceutical preparation of an oestrene derivative compound, such as tibolone, mixed with or dissolved in a pharmaceutically acceptable carrier and formulated into any one or more of various dosage forms, including "(micro)-capsules" (col. 2, line 63). Given its parenthetical form, the expression "(micro)-capsules" is taken to indicate both microcapsules and capsules, *per se*. Kelder et al. teaches a quantity of active oestrene derivative compound of "0.01 – 25 mg, usually 0.1 – 5.0 mg when the preparation is to be administered "enterally", i.e., internally (col. 2, lines 67-68). The pharmaceutically acceptable carriers disclosed by Kelder et al. include any one or more of starch, such as potato starch or corn starch, sugars, such as lactose, lubricants, such as magnesium stearate or stearic acid, or antioxidant preservatives (col.3, lines 7-16). A disclosed embodiment (see Example 1, col.4, lines 49-68) teaches the use of 2.5 mg 7α-methyl-17α-ethinyl-17β-hydroxy-Δ5(10)-oestren-3-one (also known as tibolone, see col.2, lines 48-49), 10.0 mg potato starch, 0.5 mg magnesium stearate, 0.2 mg ascorbyl palmitate, 2.0 mg amylopectin, and lactose to make up to 100 mg of the total dose unit in combination to comprise a pharmaceutical dose formulation.

The differences between the Kelder et al. reference and the presently claimed subject matter lie in that the reference does not teach:

(i) that the capsule is stabilized (see present claim 13, for example);

(ii) the use of Starch 1500, wheat starch, modified starches, agglomerated starches, and granulated starches as the water-insoluble starch product of the composition;

(iii) the use of ascorbyl stearate, sodium ascorbate or chelating agents as stabilizers;

(iv) the use of tibolone in an amount of 0.1%-10% by weight of the dosage unit (see present claim 13, for example); a pharmaceutically acceptable carrier containing lactose in an

amount of 47% to 90% by weight of the carrier (see present claim 13) and a water-insoluble starch in an amount of at least 10% to 50% by weight of the carrier (see present claim 14); or a stabilizer up to 5% by weight of the dosage unit (see present claim 16); and

(v) a method of increasing the stability of a dosage unit containing tibolone.

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) Kelder et al. teach that the compositions are to be used for pharmaceutical purposes and a person of ordinary skill in the art would have, thus, appreciated that the dosage units would, in fact, have to be stable, i.e., would not be easily decomposed or otherwise degraded. The person of ordinary skill in the art would have been motivated to use only stable dosage forms in order to ensure that the active agent was delivered to the patient in a safe and effective manner such that the intended therapeutic effect could be reasonably expected.

(ii) Although Kelder et al. expressly teaches any one or more starch ingredients, in particular, potato starch or corn starch (col.3, line 9), the reference is silent as to the use of Starch 1500, wheat starch, modified starches, agglomerated starches or granulated starches. However, wheat starch was known in the art to be synonymous with the term "starch" and was also known to be pharmaceutically acceptable (See Handbook of Pharmaceutical Excipients (1986; Section 3, entitled "Synonyms", p.289). Starch 1500 is a substance related to starch (see Section 18, entitled "Related Substances", p.293), and is, by definition, "starch that has been mechanically processed to rupture some of the granules in the presence of water and then subsequently dried".

The Handbook also teaches that "modified starches" are known in the art, typically resulting from cooked starch solutions that are readily attacked by microorganisms to form a wide variety of starch derivatives and 'modified starches' with unique physical properties (see Section 12, entitled "Stability and Storage Conditions", p.293). Agglomerated starch was also known in the art as a pharmaceutically acceptable carrier material (see de Haan, EP 0707848; 1996; p.1, lines 40-41).

Furthermore, the Examiner has noted that starch is, by its very nature, a powder composed of very small granules (see Section 9, entitled "Description", p.289), which indicates that the use of any kind of starch would meet the claim limitation of "granulated starch" as recited in present claim 16. Thus, the use of any one or more of the starches listed above as the starch product of the carrier would have been obvious to a person of ordinary skill in the art because each was well known in the art at the time of the invention and each would be reasonably expected to exert the same or similar function. Such a person would be motivated to do so in order to enhance efficacy and disintegration of the dosage unit.

(iii) Kelder et al. broadly teaches the use of antioxidant preservatives and specifically discloses the use of ascorbyl palmitate in the disclosed pharmaceutical oestrene composition (see col.3, lines 7-16 and col.4, Example 1(a)). It would, therefore, have been obvious to a person of ordinary skill in the art at the time of the invention to employ any known antioxidant preservative as a stabilizing component of the composition disclosed by Kelder et al. Loliger et al. teaches that ascorbyl stearate was a known antioxidant compound (U.S. Patent No. 5,364,886; col.1, lines 16-18). Similarly, sodium ascorbate was also well known in the art as a pharmaceutically acceptable antioxidant compound (see Handbook of Pharmaceutical

Excipients, Section 2, entitled "Functional Category", p.259). Thus, the use of such compounds well known in the art for their antioxidant function would have been well within the purview of the skilled artisan. Such a person would have been motivated to do so in order to enhance efficacy or tolerability of the compound.

Furthermore, although Kelder et al. is silent as to the use of chelating agents as stabilizers for the disclosed composition, chelators such as edetates or edetic acid were well known in the art as pharmaceutically acceptable chelators useful for forming "stable water-soluble complexes (chelates) with alkaline earth and heavy metal ions" (see Handbook of Pharmaceutical Excipients, Section 17, entitled "Applications in Pharmaceutical Formulation or Technology", p.109-110) and were also known to be antioxidant synergists (see p.110, col.1, first paragraph). Thus, because chelating agents such as edetates or edetic acid were well known in the art as having stabilizing properties as well as antioxidant properties, use of such a compound would have been obvious to the skilled artisan at the time of the invention in light of the broad teachings of Kelder et al., who discloses "antioxidant preservatives". Such a person would be motivated to do so for the reasons of record stated above in the preceding paragraph.

(iv) Kelder et al. teaches a particular embodiment of the disclosed composition in which the active compound, in this case, tibolone (see col.4, lines 49-50 and also col.2, lines 47-49), comprises 2.5 mg of the dose unit in combination with potato starch (10.0 mg), magnesium stearate (0.5 mg), ascorbyl palmitate (0.2 mg), amylopectin (2.0 mg) and lactose, in an amount to make up to 100 mg of the tablet. Thus, for a 100 mg tablet as disclosed in line 54, tibolone is 2.5%, potato starch is 10%, magnesium stearate is 0.5%, ascorbyl palmitate is 0.2%, amylopectin is 2.0% and lactose is 84.8% of the final tablet product. Thus, such a formulation meets

Applicant's definition of 0.1 to 10% by weight of tibolone, at least 10% up to 50% of starch in the carrier (see present claim 14), or up to 5% stabilizer as recited in present claim 16. Such an embodiment as disclosed by Kelder et al. teaches that the starch component, potato starch, is at least 10% of the total carrier (understood by the Examiner to be the sum of the potato starch, magnesium stearate, ascorbyl palmitate, amylopectin and lactose).

While the above example is directed to a tablet formulation, Kelder et al. broadly teach that forms suitable for enteral administration (col. 2, lines 55), including "(micro)-capsules" (col. 2, line 63), can be employed and, thus, one of ordinary skill in the art would have appreciated that the exemplified proportioning of ingredients would also apply to dosage forms other than tablets, including the presently claimed capsule dosage form. The determination of the optimum %wt of the components of the stabilized dosage formulation for other types of dosage units would have been a matter well within the purview of one of ordinary skill in the art. Such a determination would have been made in accordance with a variety of factors, such as age, weight, sex, diet and medical condition of the patient, severity of disease, route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the %wt of the components that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific %wt amounts are not seen to be inconsistent with the %wt that would have been determined by the skilled artisan.

(v) Although the disclosure of Kelder et al. is silent as to a particular method of "increasing the stability of a dosage unit containing tibolone" (see present claim 23),

pharmaceutical compositions comprised of a crystalline form of tibolone in combination with carrier materials, such as starch, ascorbyl palmitate, magnesium stearate and lactose, were known in the art to be chemically appreciably more stable that compositions comprised of a polymorphous form of tibolone in combination with carrier materials (see Sas et al., EP 0389035; 1990, p.1, lines 42-44 and Example 6, p.3, lines 35-52). Thus, it would have been obvious to a person of ordinary skill in the art at the time of the invention in light of the teachings of Sas et al. that the combination of tibolone, particularly in crystalline form, in conjunction with a carrier comprising ingredients such as starch, ascorbyl palmitate, magnesium stearate and lactose, would generate a dosage unit with increased stability and extended shelf life (see Sas et al., p.1, lines 42-44). Although Kelder et al. simply discloses tibolone, the use of a specific form of tibolone, such as a particular crystalline form, would have been encompassed by the broad teaching of tibolone and use of such was well within the purview of the skilled artisan.

Double Patenting

Obviousness-Type

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Provisional

I Claims 13-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-23 of copending U.S. Patent Application No. 10/754,685, in view of Deckers et al. (EP 0613687A1; 1994) and Kelder et al. (U.S. Patent No. 4,701,450). Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the presently claimed subject matter and the subject matter of the copending claims are the following:

(i) the present claims recite a stabilized capsule (see present claim 13, for example), while the copending claims recite a stabilized dosage unit (see copending claim 13, for example);

(ii) the present claims use lactose as a component of the carrier while the copending claims are silent as to the use of lactose;

(iii) the present claims recite an amount of the carrier comprising a water-insoluble starch product of at least 10% to 50% by weight of the carrier (see present claim 14, for example), while the copending claims recite an amount of at least 40% by weight of the carrier (see copending claims 13-15, for example);

(iv) the present claims are silent as to a quotient of the weight percentage of tibolone to starch product, while the copending claims recite a quotient of the weight percentage of tibolone to starch product of 0.02 or 0.01 (see copending claims 18-19, for example); and

(v) the present claims recite an amount of tibolone from 0.1 to 10% by weight, while the copending claims recite an amount of tibolone from 0.1 to 10% by weight or, in a particular dosage unit, 2% by weight or less (see copending claims 13 and 17, for example).

However, to the skilled artisan, the presently claimed subject matter would have been obvious because:

(i) Although the copending claims simply recite a stabilized pharmaceutical dosage unit, while the present claims expressly recite a stabilized capsule, such subject matter would have been obvious to the skilled artisan because capsules were dosage unit forms well known in the art at the time of the invention (see Deckers et al., page 1, lines 53-56) and formulation of the stabilized formulation of the copending claims into a stabilized capsule formulation would have been well within the purview of the skilled artisan.

(ii) Although the copending claims are silent as to the use of lactose in the pharmaceutically acceptable carrier used for formulating the stabilized dosage unit, use of such a compound in the carrier of the composition would have been obvious to the skilled artisan because lactose was known in the art as a component of pharmaceutically acceptable carriers (see Kelder et al., col.3, lines 7-16). Furthermore, the determination of the optimum %wt of lactose for the carrier of the composition would have been a matter well within the purview of the skilled artisan. Determination of the appropriate %wt of lactose would be reasonably expected to vary depending on the amount of active agent or the amount of starch contained in the formulation. The Examiner has also noted that the copending claims use the word "comprising", which is considered open transitional claim language and allows for the use of other components in the dose formulation recited in the copending claims (see MPEP §2111.03 [R-2] for a discussion of transitional phrases).

(iii) The determination of the optimum %wt of components of the composition recited in the copending claims would have been a matter well within the purview of the skilled artisan.

Such determination would have been made in accordance with a variety of factors, such as the age, weight, sex, and medical condition of the patient, as well as pharmacological considerations, such as toxicology and pharmacokinetics. Determination of the appropriate dose of the active agent, tibolone, would directly impact the amount of carrier necessary for formulation of the dosage unit. Thus, such an amount of carrier would be reasonably expected to vary and the amount of carrier recited in the copending claims would not be outside the scope of what would have been determined from the present claims. Furthermore, although the copending claims refer to the starch product as a "water-insoluble starch product", while the present claims simply refer to "starch product", the starch products recited in the present claims and those recited in the copending claims are the same, regardless of the way they are identified.

(iv) Although the present claims are silent as to the quotient of tibolone to starch product, the determination of the quotient of the weight percentage of tibolone to starch product would have been expected to vary depending on the amount of tibolone and the amount of starch product contained within the dosage formulation and, thus, the quotient as determined by the amounts of tibolone and starch product recited in the present claims would have been expected to be 0.02 or 0.01 at particular dosage amounts of the active components that are within the scope of the present claims. The recitation of a particular quotient is, therefore, not considered to be a patentable distinction.

(v) Although the copending claims recite the use of tibolone in an amount of 2% by weight or less in copending claim 17, the present claims recite the use of tibolone in an amount of 0.1% to 10% by weight, which clearly provides for the use of tibolone in an amount from 0.1-2.0%. The use of tibolone in an amount less than 0.1% as recited in the copending claims would

have been a determination that was well within the purview of the skilled artisan and would have been made in accordance with factors, such as the age, weight, sex and medical condition of the patient. Such is, therefore, not considered to be a patentably distinct difference between the present and the copending claims.

Claims 13-19 of the present application are not considered to be patentably distinct from copending claims 13-23 of U.S. Patent Application No. 10/754,685 and are provisionally rejected under obviousness-type double patenting.

II Claims 13-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-20 of copending U.S. Patent Application No. 10/754,733, in view of Deckers et al. (EP 0613687A1; 1994), Kelder et al. (U.S. Patent No. 4,701,450) and Stedman's Medical Dictionary (1972; p.589). Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the presently claimed subject matter and the subject matter of the copending claims are the following:

(i) the present claims recite a stabilized capsule (see present claim 13, for example), while the copending claims recite a stabilized dosage unit (see copending claim 13, for example);

(ii) the present claims use lactose as a component of the carrier (see present claim 13, for example), while the copending claims are silent as to the use of lactose;

(iii) the present claims recite an amount of the carrier comprising a water-insoluble starch product of at least 10% up to 50% by weight of the carrier (see present claim 14, for example),

while the copending claims recite an amount of at least 10% to 40% by weight of the carrier (see copending claim 13, for example);

(iv) the present claims are silent as to humid atmospheric conditions, while the copending claims recite a humid atmosphere of 50-75% relative humidity (see copending claim 13, for example); and

(v) the present claims expressly recite the use of 0.1 to 10% tibolone to be mixed with the carrier in a method of increasing the stability of a tibolone dosage unit (see present claim 19), while the copending claims do not expressly recite an amount of tibolone to be mixed with the carrier (see copending claim 20, for example).

However, to the skilled artisan, the presently claimed subject matter would have been obvious because:

(i) Although the copending claims simply recite a stabilized pharmaceutical dosage unit, while the present claims expressly recite a stabilized capsule, such subject matter would have been obvious to the skilled artisan because capsules were dosage unit forms well known in the art at the time of the invention (see Deckers et al., page 1, lines 53-56) and formulation of the stabilized formulation of the copending claims into a stabilized capsule formulation would have been well within the purview of the skilled artisan.

(ii) Although the copending claims are silent as to the use of lactose in the pharmaceutically acceptable carrier used for formulating the stabilized dosage unit, use of such a compound in the carrier of the composition would have been obvious to the skilled artisan because lactose was known in the art as a component of pharmaceutically acceptable carriers (see Kelder et al., col.3, lines 7-16). Furthermore, the determination of the optimum %wt of

lactose for the carrier of the composition would have been a matter well within the purview of the skilled artisan. Determination of the appropriate %wt of lactose would be reasonably expected to vary depending on the amount of active agent or the amount of starch contained in the formulation. The Examiner has also noted that the copending claims use the word "comprising", which is considered open transitional claim language and allows for the use of other components in the dose formulation recited in the copending claims (see MPEP §2111.03 [R-2] for a discussion of transitional phrases).

(iii) The determination of the optimum %wt of components of the composition recited in the copending claims would have been a matter well within the purview of the skilled artisan. Such determination would have been made in accordance with a variety of factors, such as the age, weight, sex, and medical condition of the patient, as well as pharmacological considerations, such as toxicology and pharmacokinetics. Determination of the appropriate dose of the active agent, tibolone, would directly impact the amount of carrier necessary for formulation of the dosage unit. Thus, such an amount of carrier would be reasonably expected to vary and the amount of carrier recited in the copending claims would not be outside the scope of what would have been determined from the present claims. Furthermore, although the copending claims refer to the starch product as a "water-insoluble starch product", while the present claims simply refer to "starch product", the starch products recited in the present claims and those recited in the copending claims are the same, regardless of the way they are identified.

(iv) Although the present claims are silent as to the presence of a humid atmosphere, the copending claims merely state that the dosage unit must be contained in a humid atmosphere until administration. Because relative humidity fluctuates as the temperature and pressure

change, it would have been apparent to the skilled artisan that conditions of 50 to 75% relative humidity would be reasonably expected to occur at any storage temperature, whether at ambient temperature or non-ambient temperature, depending on the atmospheric pressure (see Stedman's Medical Dictionary, p.589). Thus, although the present claims do not expressly recite humid atmospheric conditions of a particular relative humidity, such conditions are not considered to be outside the scope of the present claims since environmental conditions where the relative humidity was 50-75% and where the dosage unit would be subjected to such conditions would be reasonably expected to occur. Absent factual evidence to the contrary, such is not considered to be outside the scope of the present claims and the recitation of this limitation in the copending claims does not render the composition of the present claims patentably distinct from the composition of the copending claims.

(v) Although the present claims expressly recite the mixing of 0.1 to 10% tibolone in the method of increasing the stability of a dosage unit containing tibolone while the copending claims are silent as to a particular amount of tibolone to be used in this method, the copending claims expressly teach a composition comprising 0.1 to 10% tibolone. It would, therefore, have been well within the purview of the skilled artisan to employ 0.1 to 10% tibolone as recited in the copending claims in the method of increasing the stability of a dosage unit containing tibolone. Furthermore, the determination of the optimum dose of tibolone would have been a matter well within the purview of the skilled artisan and the dosages determined from the copending claims would not have been reasonably expected to differ significantly from those determined from the present claims.

Claims 13-19 of the present application are not considered to be patentably distinct from copending claims 13-20 of U.S. Patent Application No. 10/754,733 and are provisionally rejected under obviousness-type double patenting.

Non-Provisional

Claims 13-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,514,958 or claims 1-11 of U.S. Patent No. 6,399,594, in view of Deckers et al. (EP 0613687A1; 1994), Kelder et al. (U.S. Patent No. 4,701,450) and Stedman's Medical Dictionary (1972; p.589). Although the conflicting claims are not identical, they are not patentably distinct from each other because the differences between the presently claimed subject matter and the subject matter of the patented claims are the following:

(i) the present claims recite the use of a stabilized capsule (see present claim 13, for example), while the patented claims recite the use of a stabilized dosage unit (see patented claim 1 of U.S. Patent No. 6,514,958 or U.S. Patent No. 6,399,594);

(ii) the present claims recite the use of lactose as a component of the pharmaceutically acceptable carrier in an amount of at least 47% to 90% by weight of the carrier (see present claim 13, for example), while the patented claims are silent as to the use of lactose;

(iii) the present claims recite the starch product of the carrier in an amount of at least 10% to 50% by weight of the carrier (see present claim 14, for example), while the patented claims recite the starch product of the carrier in an amount of at least 40% by weight of the dosage unit (see patented claim 1 of U.S. Patent No. 6,514,958 or U.S. Patent No. 6,399,594) or at least 40%

by weight of the carrier (see patented claim 11 of U.S. Patent No. 6,514,958 or U.S. Patent No. 6,399,594);

(iv) the present claims are silent as to humid atmospheric conditions, while the patented claims of U.S. Patent No. 6,514,958 recite a humid atmosphere of 50-70% relative humidity (see patented claim 1, for example);

(v) the present claims recite an amount of tibolone from 0.1 to 10% by weight, while the patented claims recite a particular dosage unit where tibolone is in an amount of 2% by weight or less (see patented claim 5 of either U.S. Patent No. 6,514,958 or 6,399,594); and

(vi) the present claims are silent as to a quotient of tibolone to starch product of 0.02 or 0.01 (see patented claims 6-7, for example, of either U.S. Patent No. 6,514,958 or 6,399,594).

However, to the skilled artisan, the presently claimed subject matter would have been obvious because:

(i) Although the patented claims simply recite a stabilized pharmaceutical dosage unit, while the present claims expressly recite a stabilized capsule, such subject matter would have been obvious to the skilled artisan because capsules were dosage unit forms well known in the art at the time of the invention (see Deckers et al., page 1, lines 53-56) and formulation of the stabilized formulation of the patented claims into a stabilized capsule formulation would have been well within the purview of the skilled artisan.

(ii) Although the patented claims are silent as to the use of lactose in the pharmaceutically acceptable carrier used for formulating the stabilized dosage unit, use of such a compound in the carrier of the composition would have been obvious to the skilled artisan because lactose was known in the art as a component of pharmaceutically acceptable carriers

(see Kelder et al., col.3, lines 7-16). Furthermore, the determination of the optimum %wt of lactose for the carrier of the composition would have been a matter well within the purview of the skilled artisan. Determination of the appropriate %wt of lactose would be reasonably expected to vary depending on the amount of active agent or the amount of starch contained in the formulation. The Examiner has also noted that the patented claims use the word "comprising", which is considered open transitional claim language and allows for the use of other components in the dose formulation recited in the patented claims (see MPEP §2111.03 [R-2] for a discussion of transitional phrases).

(iii) The determination of the optimum %wt of components of the composition recited in the present claims would have been a matter well within the purview of the skilled artisan. Such determination would have been made in accordance with a variety of factors, such as the age, weight, sex, and medical condition of the patient, as well as pharmacological considerations, such as toxicology and pharmacokinetics. Determination of the appropriate dose of the active agent, tibolone, would directly impact the amount of carrier necessary for formulation of the dosage unit. Thus, such an amount of carrier would be reasonably expected to vary and the amount of carrier recited in the present claims would not be outside the scope of what would have been determined from the patented claims. Furthermore, although the patented claims refer to the starch product as a "water-insoluble starch product", while the present claims simply refer to "starch product", the starch products recited in the present claims and those recited in the patented claims are the same, regardless of the way they are identified.

In addition, the amount of the starch product of the patented claims is given as a % by weight of the dosage unit (see patented claim 1 of either U.S. Patent No. 6,514,958 or

6,399,594), while the amount of the present claims is given as a % by weight of the carrier. However, such is not considered to be a patentably distinct difference between the compositions because the dosage formulation is primarily comprised of the pharmaceutically acceptable carrier, so the difference between a % by weight of the dosage unit versus a % by weight of the carrier would not result in a major difference in the weight of the carrier of either composition.

(iv) Although the present claims are silent as to the presence of a humid atmosphere, the patented claims of U.S. Patent No. 6,514,958 merely state that the dosage unit must be contained in a humid atmosphere until administration. Because relative humidity fluctuates as the temperature and pressure change, it would have been apparent to the skilled artisan that conditions of 50 to 70% relative humidity would be reasonably expected to occur at any storage temperature, whether at ambient temperature or non-ambient temperature, depending on the atmospheric pressure (see Stedman's Medical Dictionary, p.589). Thus, although the present claims do not expressly recite humid atmospheric conditions of a particular relative humidity, such conditions are not considered to be outside the scope of the present claims since environmental conditions where the relative humidity was 50-70% and where the dosage unit would be subjected to such conditions would be reasonably expected to occur. Absent factual evidence to the contrary, such is not considered to be outside the scope of the present claims and the recitation of this limitation in the patented claims does not render the composition of the present claims patentably distinct from the composition of the patented claims.

(v) Although the patented claims recite the use of tibolone in an amount of 2% by weight or less (see patented claim 5 of either U.S. Patent No. 6,514,958 or 6,399,594), the present claims recite the use of tibolone in an amount of 0.1% to 10% by weight, which clearly provides

for the use of tibolone in an amount from 0.1-2.0%. The use of tibolone in an amount less than 0.1% as recited in the patented claims would have been a determination that was well within the purview of the skilled artisan and would have been made in accordance with factors, such as the age, weight, sex and medical condition of the patient. Such is, therefore, not considered to be a patentably distinct difference between the present and the patented claims.

(vi) Although the present claims are silent as to the quotient of tibolone to starch product, the determination of the quotient of the weight percentage of tibolone to starch product would have been expected to vary depending on the amount of tibolone and the amount of starch product contained within the dosage formulation and, thus, the quotient as determined by the amounts of tibolone and starch product recited in the present claims would have been expected to be 0.02 or 0.01 at particular dosage amounts of the active components that are within the scope of the present claims. The recitation of a particular quotient is, therefore, not considered to be a patentable distinction.

Claims 13-19 of the present application are not considered to be patentably distinct from claims 1-11 of U.S. Patent No. 6,514,958 or claims 1-11 of U.S. Patent No. 6.399,594 and are rejected under obviousness-type double patenting.

Conclusion

Rejection of claims 13-19 is deemed proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (8:30 AM-6:00 PM), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 29, 2005

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